

REMARKS/ARGUMENTS

Claims 16-25 are active. Minor edits have been made to improve the clarity of the claims. No new matter has been added.

Aspects of the Invention

The claimed invention is directed to a method of producing chemiluminescence in a solid phase immunoassay, comprising contacting at least one antigen or/and an antibody immobilized onto fine solid carriers dispersed in a liquid medium with a chemiluminescent substrate comprising at least one dioxetane, an enzyme for performing chemiluminescence, and a chemiluminescence enhancer comprising a water soluble macromolecular quaternary ammonium salt, a water soluble macromolecular sulfonium salt or a water soluble macromolecular quaternary phosphonium salt each of which has been treated with an oxidizing agent or a reducing agent. **By using the chemiluminescence enhancer of the present invention, dispersibility of fine solid carriers in a chemiluminescence reaction is improved compared to conventional chemiluminescence enhancers, enhancement of chemiluminescence and within-run reproducibility (CV value) is achieved and more precise quantification becomes possible as described by Examples 1-7 of the present specification.**

Rejection—35 U.S.C. §103

Claims 16-25 were rejected under 35 U.S.C. 103(a) as being unpatentable over Bronstein et al., U.S. Patent No. 5,753,436, in view of Akhavan-Tafti et al., U.S. Patent No. 6,045,727.

While Bronstein et al. (US 5,753,436) disclose a “chemiluminescence enhancer”, this document describes a quaternary ammonium, phosphonium or sulfonium salt chemiluminescence enhancer, which is different from a chemiluminescence enhancer which

has been treated with an oxidizing agent or a reducing agent as required by the present invention.

There is no suggestion or reasonable expectation of success for the superior properties of the chemiluminescence enhancers of the invention in Bronstein. These superior properties are demonstrated by the comparisons between a chemiluminescence enhancer of Bronstein et al. and a chemiluminescence enhancer of the present invention are described in Examples 1-7 of the present specification. For example, table 1 on page 14 of the present specification shows that, the treated TBQ groups corresponding to a chemiluminescence enhancer of the present invention increased the luminescence and enhanced within-run reproducibility (CV value), that is, led to the enhancement and stabilization of luminescence as compared to the untreated TBQ corresponding to a chemiluminescence enhancer of Bronstein et al. As shown, the effects of the present invention in chemiluminescence method using the fine solid carriers are extremely superior to that of the method of Bronstein et al.

Akhaven-Tafti et al. was cited as teaching a chemiluminescence method which includes "the addition of an effective amount of a background reducing agent (oxidizing or reducing) to the chemiluminescent composition". However, as detailed below, there is no suggestion in this document for the present invention, this document provides no motivation for combining its teachings with those of the primary reference because it employs different reagents and uses certain components for different reasons. Moreover, there is no reasonable expectation of success for the superior results obtained by the present inventions in Akhaven-Tafti et al.

Constituent comparison between a reagent for chemiluminescence described in Akhaven-Tafti et al. and a reagent of the present invention (Claim 16) is as follows:

Constituent	Claim 16 of the present invention	Akhaven-Tafti et al. (Column 21, line 45...)
Chemiluminescent substrate	dioxetane	Compound of formula I-V (Not dioxetane compounds)
Chemiluminescence enhancer	A water soluble macromolecular quaternary ammonium salt, a water soluble macromolecular sulfonium salt or a water soluble macromolecular quaternary phosphonium salt chemiluminescence enhancer treated with an oxidizing agent or a reducing agent	Anionic surfactant (SDS) and non-ionic surfactant (Tween 20)  (SDS is not a water soluble <u>macromolecular</u> sulfonium salt.)
Compounds having oxidation/reduction potential suitable for causing an increase in chemiluminescence	-	Cationic aromatic compound (CAC): cyan dyes, thiacyanine dyes, carbocyanine dyes...
Background reducing agents	-	Sulfite salts (lithium sulfite, sodium sulfite, potassium sulfite)
Effects		
	Improvement in dispersibility of fine solid carriers and increase in within-run reproducibility (CV value)	Sulfite salts prevent the accumulation of background chemiluminescence and reduce the background amount.

Akhaven-Tafti et al. discloses a chemiluminescence enhancer comprising a surfactant for the addition to a chemiluminescent substrate of formula I-V mentioned at column 14, lines 49-67 and column 15, lines 1-36 of the reference. Also there is disclosed that, when anionic surfactants or nonionic surfactants are used as a chemiluminescence enhancer, CAC suitable for causing an increase in chemiluminescence and sulfite salts as a reagent for reducing background amount are further added to the chemiluminescent substrate mentioned at column 21, lines 45-63.

In Akhaven-Tafti et al., sulfite salts are added to chemiluminescence substrate as a background reducing agent as mentioned at column 21, lines 45-63, while in the present invention, sulfite salts are used to treat a chemiluminescence enhancer. The Examiner said that it would have been obvious to one of ordinary skill in the art to include with the method of Bronstein et al. the treatment with a background reducing agent, i.e. oxidizing or reducing agent, as taught by Akhavan-Tafti et al. However, Akhaven-Tafti et al. does not disclose or suggest the treatment of a chemiluminescence enhancer with an oxidizing agent or a reducing agent.

In addition, the chemiluminescence enhancer of Akhaven-Tafti et al. is not used for a chemiluminescent substrate comprising dioxetane. As can be seen from the above table, a constitution of chemiluminescence enhancer and constituent of reagents, etc. used in chemiluminescence measurements of the present invention is completely different from those of Akhaven-Tafti et al.


Furthermore, the cited prior art provides no motivation for combining the teachings of Bronstein et al. and Akhaven-Tafti et al. The effect of Akhaven-Tafti et al. is to prevent accumulation of background chemiluminescence, while the effect of the present invention is to improve dispersibility of fine solid carriers and increase within-run reproducibility (CV value) at a time of measurement. Accordingly, the cited prior art does not suggest or provide a reasonable expectation of success for the present invention and, therefore, the Applicants respectfully request that this rejection be withdrawn.

CONCLUSION

In view of the remarks above, the Applicants respectfully submit that this application is now in condition for allowance. An early notice to that effect is earnestly solicited.

Respectfully submitted,

OBLON, SPIVAK, McCLELLAND,  
MAIER & NEUSTADT, P.C.  
Norman F. Oblon

  
Thomas M. Cunningham  
Registration No. 45,394

Customer Number

**22850**

Tel: (703) 413-3000  
Fax: (703) 413 -2220  
(OSMMN 06/04)